

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing  
(day/month/year)

1 0. 05. 99

Applicant's or agent's file reference  
P1066P2

IMPORTANT NOTIFICATION

International application No.  
PCT/US98/01774

International filing date (day/month/year)  
30/01/1998

Priority date (day/month/year)  
07/02/1997

Applicant  
GENENTECH, INC. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.


4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

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# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT



(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>P1066P2</b>		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US98/01774</b>	International filing date (day/month/year) <b>30/01/1998</b>	Priority date (day/month/year) <b>07/02/1997</b>	
International Patent Classification (IPC) or national classification and IPC <b>C12N15/12</b>			
Applicant <b>GENENTECH, INC. et al.</b>			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.  
  
☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
  
 These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  <b>16/07/1998</b>	Date of completion of this report  <b>1 0. 05. 99</b>
Name and mailing address of the international preliminary examining authority:   <b>European Patent Office</b> <b>D-80298 Munich</b> <b>Tel. (+49-89) 2399-0 Tx: 523656 epmu d</b> <b>Fax: (+49-89) 2399-4465</b>	Authorized officer  <b>Vollbach, S</b>   <b>Telephone No. (+49-89) 2399 8715</b>

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US98/01774

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-85 as originally filed

**Claims, No.:**

1-22 as received on 23/12/1998 with letter of 21/12/1998

**Drawings, sheets:**

1/23-23/23 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.  
☒ claims Nos. 10.

because:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US98/01774

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 10 are so unclear that no meaningful opinion could be formed (*specify*):
- see separate sheet**
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims 2,3,
	No:	Claims 1,4-9,11-22
Inventive step (IS)	Yes:	Claims 2,3,
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-22
	No:	Claims

**2. Citations and explanations**

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

1. The present application relates to a new substrate protein (PSTPIP) for the known PST HSCF tyrosine phosphatase, an antagonist of said PSTPIP polypeptide, an antibody and methods for its production and use.

2. None of the cited documents discloses or suggest the specific PSTPIP polypeptide. Therefore the present application is considered to contain patentable subject-matter.

3. However, the following objections apply to present set of claims. The claims are not restricted to the specific protein for which novelty and inventiveness is acknowledged. Instead the claims in its broadest sense also cover functional derivatives of said protein. The definition "peptides encoded by nucleic acid which hybridizes under stringent conditions to nucleic acid shown in Seq. D No:1 provided that it retains the ability to bind to a PEST-type protein tyrosine phosphatase" embraces e.g. the CDC15p a Schizosaccharomyces pombe phosphoprotein cited in the description of the present application, as well as the p130cas protein from Hela cells which is disclosed in D1: Molecular and Cellular Biology, vol. 16, No. 11, 1996). Therefore claim 1 contains subject-matter not allowed under Article 33(2) PCT. The same objection also apply to present claims 4,5-9. Since the nucleic acid claims, the antibody claims and the method claims refer back to the protein claims the same lack of novelty objection also apply to said claims (present claims 11-18, 19-22).

Moreover, claim 10 which relates to an antagonist of PSTPIP is objectionable under Article 6 PCT because said claim is totally unclear. Without any technical features defining the antagonist, said antagonist can also be a known compound. Therefore, before an examination with regard to said claim can be carried out the antagonist need to be specified.

4. In summary, the present claims are broadened in a manner that non-novel subject-matter is embraced by said claims.

When drafting new claims, the following vague expressions should be avoided:

The vague definition used in claim 1 item (iii) is unclear and thus objectionable under Article 6 PCT.

5. The applicant is informed that if the priority claimed in the present application is

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US98/01774

not valid, an intermediate document becomes highly relevant for the assessment of novelty of the claims.

Claims:

1. An isolated PSTPIP polypeptide selected from the group consisting of:

(i) a polypeptide comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO:1);

(ii) a polypeptide having at least 65% sequence homology with the PSTPIP amino acid sequence of Fig. 1A (SEQ ID NO:1); and

(iii) a polypeptide encoded by nucleic acid which hybridizes under stringent conditions to nucleic acid encoding the polypeptide of (i);

provided that the polypeptides of (ii) and (iii) substantially retain the ability to bind to a member of the PEST-type protein tyrosine phosphatases.

2. The PSTPIP polypeptide of Claim 1 having at least 85% sequence homology with the PSTPIP amino acid sequence of Fig. 1A (SEQ ID NO:1).

3. The PSTPIP polypeptide of Claim 1 comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig 1A (SEQ ID NO:1).

4. The PSTPIP polypeptide of Claim 1 which is capable of being dephosphorylated by a member of the PEST-type protein tyrosine phosphatases when phosphorylated on at least one tyrosine residue.

5. The PSTPIP polypeptide of Claim 1, wherein the member of the PEST-type protein tyrosine phosphatases is PTP HSCF.

6. The PSTPIP polypeptide of Claim 1 which is devoid of a C-terminal SH3 domain.
- 5 7. The PSTPIP polypeptide of Claim 1 which is not phosphorylated.
8. The PSTPIP polypeptide of Claim 1 which is phosphorylated on at least one tyrosine residue.
- 10 9. The PSTPIP polypeptide of Claim 1 which associates with actin.
10. An antagonist of the PSTPIP polypeptide of Claim 1.
- 15 11. An isolated nucleic acid sequence which encodes the PSTPIP polypeptide of Claim 1.
12. A vector comprising the nucleic acid sequence of Claim 11 operably linked to control sequences recognised by a host cell transformed with the vector.
- 20 13. A host cell comprising the nucleic acid sequence of Claim 11.
- 25 14. A host cell comprising the vector of Claim 12.
15. An antibody capable of specific binding to the PSTPIP polypeptide of Claim 1.
- 30 16. The antibody of Claim 15 which is detectably labeled.
17. The antibody of Claim 15 which is a monoclonal antibody.
18. A hybridoma cell line which produces the antibody of Claim 15.
- 35 19. A method for producing the PSTPIP polypeptide of Claim 1



comprising transforming a host cell with nucleic acid encoding said polypeptide, culturing the transformed cell and recovering said polypeptide from the cell culture.

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20. A method for inducing the polymerization of actin monomers in a eukaryotic cell comprising introducing into said cell the PSTPIP polypeptide of Claim 1.

10

21. The method of Claim 20, wherein the step of introducing comprises introducing into said cell the vector of Claim 13.

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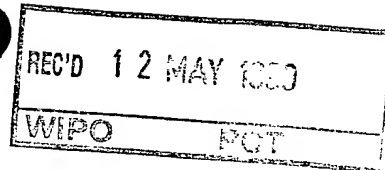
22. An assay for identifying an antagonist or agonist of the PSTPIP polypeptide of Claim 1 which comprises contacting the PSTPIP polypeptide of Claim 1 with a candidate antagonist or agonist and monitoring the ability of said polypeptide to induce the polymerization of actin monomers.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



19

Applicant's or agent's file reference P1066P2	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
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Date of submission of the demand 16/07/1998	Date of completion of this report 10.05.99
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Vollbach, S Telephone No. (+49-89) 2399 8715 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US98/01774

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**INTERNATIONAL PRELIMINARY  
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International application No. PCT/US98/01774

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**see separate sheet**

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Inventive step (IS)	Yes: Claims 2,3, No: Claims
Industrial applicability (IA)	Yes: Claims 1-22 No: Claims

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**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US98/01774

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**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US98/01774

not valid, an intermediate document becomes highly relevant for the assessment of novelty of the claims.

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/01774

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/47 G01N33/50 C07K16/18 C12N5/20

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	SPENCER S ET AL: "PSTPIP: a tyrosine phosphorylated cleavage furrow-associated protein that is a substrate for a PEST tyrosine phosphatase." J CELL BIOL, AUG 25 1997, 138 (4) P845-60, UNITED STATES, XP002068211 cited in the application see the whole document	1-23
T	WU Y ET AL: "Tyrosine phosphorylation regulates the SH3-mediated binding of the Wiskott-Aldrich syndrome protein to PSTPIP, a cytoskeletal-associated protein." J BIOL CHEM, MAR 6 1998, 273 (10) P5765-70, UNITED STATES, XP002068212 --- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

16 June 1998

Date of mailing of the international search report

30/06/1998

Name and mailing address of the ISA

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Authorized officer

Espen, J

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/01774

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DOSIL M ET AL: "CLONING AND CHARACTERIZATION OF FETAL LIVER PHOSPHATASE 1, A NUCLEAR PROTEIN TYROSINE PHOSPHATASE ISOLATED FROM HEMATOPOIETIC STEM CELLS" BLOOD, vol. 88, no. 12, 15 December 1996, pages 4510-4525, XP002034267 see page 4512, left-hand column ----	11
A	GARTON A J ET AL: "IDENTIFICATION OF 130CAS AS A SUBSTRATE FOR THE CYTOSOLIC PROTEIN TYROSINE PHOSPHATASE PTP-PEST" MOLECULAR AND CELLULAR BIOLOGY, vol. 16, no. 11, November 1996, pages 6408-6418, XP002051430 cited in the application ----	
A	CLOUTIER JF ET AL: "Association of inhibitory tyrosine protein kinase p50csk with protein tyrosine phosphatase PEP in T cells and other hemopoietic cells" EMBO JOURNAL, vol. 15, no. 18, 1996, EYNSHAM, OXFORD GB, pages 4909-4918, XP002068213 cited in the application -----	





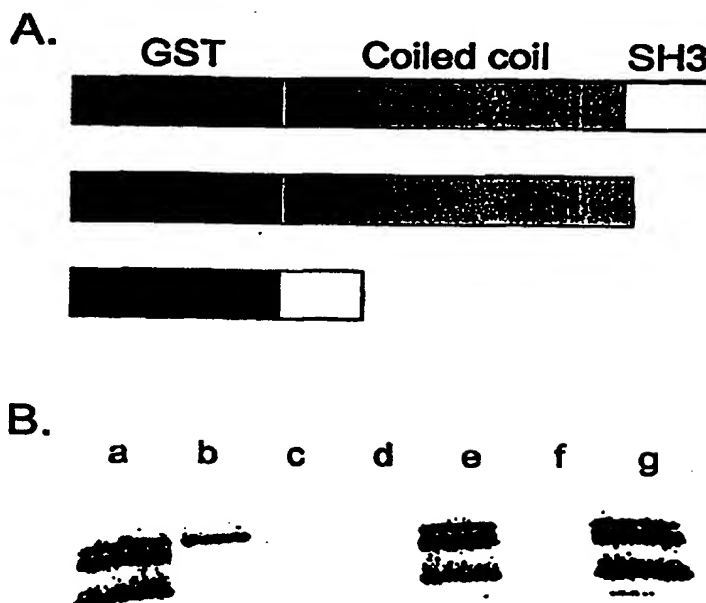
## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>C12N 15/12, C07K 14/47, G01N 33/50, C07K 16/18, C12N 5/20</b>		A1	(11) International Publication Number: <b>WO 98/35037</b>
			(43) International Publication Date: 13 August 1998 (13.08.98)
(21) International Application Number: PCT/US98/01774		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 30 January 1998 (30.01.98)		<b>Published</b> <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(30) Priority Data: 08/798,419 7 February 1997 (07.02.97) US 08/938,829 29 September 1997 (29.09.97) US			
(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 08/938,829 (CIP) Filed on 29 September 1997 (29.09.97)			
(71) Applicant (for all designated States except US): GENENTECH, INC. [US/US]; 1 DNA Way, South San Francisco, CA 94080-4990 (US).			
(72) Inventors; and (75) Inventors/Applicants (for US only): LASKY, Laurence, A. [US/US]; Star Route, Box 460, Sausalito, CA 94965 (US). DOWBENKO, Donald, J. [US/US]; 456 Elm Avenue, San Bruno, CA 94066 (US).			
(74) Agents: DREGER, Ginger, R. et al.; Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990 (US).			

(54) Title: TYROSINE PHOSPHORYLATED CLEAVAGE FURROW-ASSOCIATED PROTEINS (PSTPIPs)

## (57) Abstract

This invention concerns new PST-PIP polypeptides which are bound by and dephosphorylated by the PEST family of protein tyrosine phosphatases. The invention specifically concerns native murine PSTPIP polypeptides and their homologues in other mammals, and their functional derivatives. The invention further relates to nucleic acids encoding these proteins, vectors containing and capable of expressing such nucleic acid, and recombinant host cells transformed with such nucleic acid. Methods for inducing the polymerization of actin monomers in eukaryotic cells and assays for identifying antagonists and agonists of the PSTPIP polypeptides of the present invention are also provided.



**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

Replaced by AHID 08 May 98

WHAT IS CLAIMED IS:

1. An isolated PSTPIP polypeptide selected from the group consisting of:
  - (i) a polypeptide comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO:1);
  - (ii) a further mammalian homologue of the polypeptide of (i);
  - (iii) a polypeptide encoded by nucleic acid which hybridizes under stringent conditions to nucleic acid encoding the polypeptide of (i) or (ii) and which substantially retains the ability to bind to a member of the PEST-type protein tyrosine phosphatases; and
  - (iv) a functional derivative of any of the polypeptides (i)-(iii) substantially retaining the ability to bind to a member of the PEST-type protein tyrosine phosphatases.
2. The PSTPIP polypeptide of Claim 1 comprising the amino acid sequence of the PSTPIP polypeptide shown in Fig. 1A (SEQ ID NO:1).
3. The PSTPIP polypeptide of Claim 1 which is capable of being dephosphorylated by a member of the PEST-type protein tyrosine phosphatases when phosphorylated on at least one tyrosine residue.
4. The PSTPIP polypeptide of Claim 1, wherein the member of the PEST-type protein tyrosine phosphatases is PTP HSCF.
5. The PSTPIP polypeptide of Claim 1 which is of murine origin.
6. The PSTPIP polypeptide of Claim 1 which is of human origin.
7. The PSTPIP polypeptide of Claim 1 which is devoid of a C-terminal SH3 domain.
8. The PSTPIP polypeptide of Claim 1 which is not phosphorylated.
9. The PSTPIP polypeptide of Claim 1 which is phosphorylated on at least one tyrosine residue.
10. The PSTPIP polypeptide of Claim 1 which associates with actin.
11. An antagonist of the PSTPIP polypeptide of Claim 1.
12. An isolated nucleic acid sequence which encodes the PSTPIP polypeptide of Claim 1.
13. A vector comprising the nucleic acid sequence of Claim 12 operably linked to control sequences recognized by a host cell transformed with the vector.
14. A host cell comprising the nucleic acid sequence of Claim 12.
15. A host cell comprising the vector of Claim 13.
16. An antibody capable of specific binding to the PSTPIP polypeptide of Claim 1.
17. The antibody of Claim 16 which is detectably labeled.
18. The antibody of Claim 16 which is a monoclonal antibody.
19. A hybridoma cell line which produces the antibody of Claim 16.
20. A method for producing the PSTPIP polypeptide of Claim 1 comprising transforming a host cell with nucleic acid encoding said polypeptide, culturing the transformed cell and recovering said polypeptide from the cell culture.
21. A method for inducing the polymerization of actin monomers in a eukaryotic cell comprising introducing into said cell the PSTPIP polypeptide of Claim 1.

22. The method of Claim 21, wherein the step of introducing comprises introducing into said cell the vector of Claim 13.

23. An assay for identifying an antagonist or agonist of the PSTPIP polypeptide of Claim 1 which comprises contacting the PSTPIP polypeptide of Claim 1 with a candidate antagonist or agonist and  
5 monitoring the ability of said polypeptide to induce the polymerization of actin monomers.

## P, ENT COOPERATION TREA

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## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
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Crystal Plaza 2  
Washington, DC 20231  
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in its capacity as elected Office

Date of mailing: 13 August 1998 (13.08.98)	Applicant's or agent's file reference: P1066P2
International application No.: PCT/US98/01774	Priority date: 07 February 1997 (07.02.97)
International filing date: 30 January 1998 (30.01.98)	
Applicant: LASKY, Laurence, A. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International preliminary Examining Authority on:  
16 July 1998 (16.07.98)☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Form PCT/IB/331 (July 1992)

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

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5620

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

09/068.377

Applicant's or agent's file reference <b>P1066P2</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/US 98/01774</b>	International filing date (day/month/year) <b>30/01/1998</b>	(Earliest) Priority Date (day/month/year) <b>07/02/1997</b>
Applicant <b>GENENTECH, INC. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☐ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☒ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☒ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☒ the text is approved as submitted by the applicant

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. 5 ☒ as suggested by the applicant.

☐ None of the figures.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 98/01774

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C07K14/47 G01N33/50 C07K16/18 C12N5/20

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C07K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	SPENCER S ET AL: "PSTPIP: a tyrosine phosphorylated cleavage furrow-associated protein that is a substrate for a PEST tyrosine phosphatase." J CELL BIOL, AUG 25 1997, 138 (4) P845-60, UNITED STATES, XP002068211 cited in the application see the whole document ---	1-23
T	WU Y ET AL: "Tyrosine phosphorylation regulates the SH3-mediated binding of the Wiskott-Aldrich syndrome protein to PSTPIP, a cytoskeletal-associated protein." J BIOL CHEM, MAR 6 1998, 273 (10) P5765-70, UNITED STATES, XP002068212 --- -/--	

☒ Further documents are listed in the continuation of box C.☐ Patent family members are listed in annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

16 June 1998

Date of mailing of the international search report

30/06/1998

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/01774

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DOSIL M ET AL: "CLONING AND CHARACTERIZATION OF FETAL LIVER PHOSPHATASE 1, A NUCLEAR PROTEIN TYROSINE PHOSPHATASE ISOLATED FROM HEMATOPOIETIC STEM CELLS" BLOOD, vol. 88, no. 12, 15 December 1996, pages 4510-4525, XP002034267 see page 4512, left-hand column ---	11
A	GARTON A J ET AL: "IDENTIFICATION OF 130CAS AS A SUBSTRATE FOR THE CYTOSOLIC PROTEIN TYROSINE PHOSPHATASE PTP-PEST" MOLECULAR AND CELLULAR BIOLOGY, vol. 16, no. 11, November 1996, pages 6408-6418, XP002051430 cited in the application ---	
A	CLOUTIER JF ET AL: "Association of inhibitory tyrosine protein kinase p50csk with protein tyrosine phosphatase PEP in T cells and other hemopoietic cells" EMBO JOURNAL, vol. 15, no. 18, 1996, EYNSHAM, OXFORD GB, pages 4909-4918, XP002068213 cited in the application -----	